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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/982,113	10/17/2001	Gabriel Lopez-Berestein	UTSC:660US/SLH	9331

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1615	12

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/982,113	Applicant(s) Berestein
	Examiner Gollamudi Kishore	Art Unit 1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 20, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-130* is/are pending in the application.

4a) Of the above, claim(s) *1-55 and 61-130* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *56-60* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *6 and 7*
4) ☒ Interview Summary (PTO-413) Paper No(s). *11*
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election without traverse of Group III, and species in claims 54-60 in Paper No. 10 and during subsequent telephone conversation on 6-4-03 (for the species) is acknowledged.

Claims included in the prosecution are 54-60. Although as discussed below, claim 58 depends from itself, since it appears that the applicant's intent is to make it dependent from claim 57, said claim 58 is included in the prosecution.

Claim Rejections - 35 USC § 112

2.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 58 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 58 depends from itself and therefore, indefinite.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the**

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 54-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mehta (5,811,119) in view of Ulukaya (Cancer Treatment Reviews, 25, pp. 229-235, 1999 of record.

Mehta discloses a method of treatment of cancer using liposomal retinoid. The liposomes are made from the claimed combination of dimyristoyl phosphatidyl choline and the intercalation promoter, soybean oil (note the abstract, col. 3, lines 16-21; col. 6, line 24 through col. 7, line 31; Examples, in particular Examples 1, 5, 6 and 9. Although in Mehta, the invention is exemplified using retinoic acid, according to Mehta on col. 2, line 60 et seq., the term includes all retinoids.

Mehta however, does not specifically teach 4 hydroxyphenyl retinamide.

Ulukaya while disclosing the relationship between 4 hydroxyphenyl retinamide and cancer, teaches that this retinoid has fewer side effects compared to naturally occurring retinoids and that it seems to induce apoptosis via different pathway from classical retinoids (note the abstract).

The use of 4-hydroxyphenyl retinamide as the specific retinoid in the teachings of Mehta would have been obvious to one of ordinary skill in the art since Mehta teaches the use of any retinoid and Ulukaya teaches that this retinoid has fewer side effects compared to naturally occurring retinoids and induces apoptosis via different pathway from classical retinoids.

6. Claims 54-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mehta (5,811,119) in view of Minton (5,008,291) or Zeligs (6,093,706) by themselves OR vice versa: that is, Minton (5,008,291), or Zeligs (6,093,706) in view of Mehta (5,811,119).

Mehta discloses a method of treatment of cancer using liposomal retinoid. The liposomes are made from the claimed combination of dimyristoyl phosphatidyl choline and the intercalation promoter, soybean oil (note the abstract, col. 3, lines 16-21; col. 6, line 24 through col. 7, line 31; Examples, in particular Examples 1, 5, 6 and 9. Although in Mehta, the invention is exemplified using retinoic acid, according to Mehta on col. 2, line 60 et seq., the term includes all retinoids.

Minton in 291 teaches that a combination method for achieving a very high degree of chemotherapeutic activity through a synergistic combination of a low suboptimal dose of calcium glucarate (anti-carcinogen) and a suboptimal dose of 4-hydroxyphenyl retinamide. One of the cancers studied is mammary cancer (abstract; col.4, line 23 through col. 6, line 41; Examples). What is lacking in Minton is the use of liposomes as the sustained release carriers for the combination. However, Minton on col. 13, lines 17 and 18 suggests the use of sustained or continuous release formulations.

Zeligs teaches a combination treatment of diseases such as squamous cell carcinoma using 4-hydroxyphenyl retinamide and dehydroepiandrosterone. The combination is administered in the form of liposomes (abstract, col. 5, line 28; col. 6, line 60; Example 3;

claims 46 and 55). What is lacking in Zeligs' liposomes is the use of DMPC as the phospholipid and the inclusion of soybean oil.

It would have been obvious to one of ordinary skill in the art to use 4-hydroxyphenyl retinamide as the specific retinoid in the teachings of Mehta since Mehta teaches the use of any retinoid and the references of Minton and Zeligs show the effectiveness of this retinoid in combination with other active agents which includes synergism as noted from Minton. Alternately, the use of liposomes containing DMPC and soybean oil of Mehta as the sustained release carriers for the formulations of Minton, or Zeligs would have been obvious to one of ordinary skill in the art since this combination of DMPC and the intercalation promoter, soybean oil is very effective for the delivery of retinoids in cancer treatment process as taught by Mehta.

7. Claims 57-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mehta (5,811,119) in view of Ulukaya (Cancer Treatment Reviews, 25, pp. 229-235, 1999 of record as set forth above, further in view of Minton (5,008,291), or Zeligs (6,093,706).

The teachings of Mehta, Ulukaya, Minton and Zeligs have been discussed above. What is lacking in Mehta is the teaching of the administer the composition in combination with an additional agent.

As pointed out above, Minton, and Zeligs teach the combination of 4-hydroxyphenyl retinamide with glucarolactone and DHEA respectively.

It would have been obvious to one of ordinary skill in the art to include an additional agent in the compositions of Mehta since the references of Minton and Zeligs show the effectiveness of this retinoid in combination with other active agents which includes synergism as noted from Minton.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.

Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

gsk

June 10, 2003